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EXAMINER	
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ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,392	YU ET AL.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-8,10-14,16-20 and 22-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 5-8, 10, 11, 12, 13, 16-20, 22 -27* is/are rejected.

7)☒ Claim(s) *1,5,8,14,16,17,22,23 and 27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/21/08 has been entered.

Claims 1, 2, 5-8, 10-14, 16-20, and 22-27 are pending.

Claims 1, 2, 5, 8, 12-14, 16, 17, 22-24, and 27 have been amended by Applicant.

Claims 1, 2, 5-8, 10-14, 16-20, and 22-27 are currently under consideration.

This Office Action contains new rejections.

Objections Withdrawn

All previous objections are withdrawn.

Rejections Withdrawn

All previous rejections are withdrawn.

New Objection

Claims 1 and 16 are objected to for apparent typographical errors. Claims 1 and 16 recite: "…(SEQ ID NOS: 2-5, exonuclease…". There appears to be a missing right

parenthesis after "2-5". The following amendment would obviate this objection: "…(SEQ ID NOS: 2-5**)**, exonuclease…". Proper correction is required.

Claim 1 is objected to for an apparent typographical error. Claim 1 recites: "…the step of determining least one status…". The word "at" appears to be missing between "determining" and "least". The following amendment would obviate this objection: "…the step of determining **at** least one status…". Proper correction is required.

Claim 5 is objected to for awkwardly reciting: "…measuring the levels of said nucleic acid expression products in the sample of the genes of the prognostic set, thereby obtaining an expression profile". The phrase "of the genes of the prognostic set" seems to be out of place. The following amendment would obviate this objection: "…measuring the levels of said nucleic acid expression products in the sample ~~**of the genes of the prognostic set**~~, thereby obtaining an expression profile". Proper correction is required.

Claim 8 is objected to for an apparent typographical error. Claim 8 recites: "…either high Nottingham Prognostic Index (NPI) or low, or as either…". The word "NPI" appears to be missing after the word "low". The following amendment would obviate this objection: "…either high Nottingham Prognostic Index (NPI) or low **NPI**, or as either…". Proper correction is required.

Claim 17 is objected to for an apparent typographical error. Claim 17 recites: "…or all of nucleic acids encoded by…". The word "the" appears to be missing between "of" and "nucleic". The following amendment would obviate this objection: "…or all of **the** nucleic acids encoded by…". Proper correction is required.

Claim 22 is objected to for an apparent typographical error. Claim 22 recites: "…said kit comprising a no more than 500…". The word "a" appears to be out of place. The following amendment would obviate this objection: "…said kit comprising ~~a~~ no more than 500…". Proper correction is required.

Claims 22 and 23 are objected to for apparent typographical errors. Claims 22 and 23 recite: "…MCM4 minichromosome maintenance deficient 4 (S. cerevisiae) (SEQ ID NO: 2-6)…". SEQ ID NO:6 is exonuclease 1 and is not representative of MCM4 minichromosome maintenance deficient 4 (S. cerevisiae) . The following amendment would obviate this objection: "…MCM4 minichromosome maintenance deficient 4 (S. cerevisiae) (SEQ ID NO: 2-~~6~~**5**)…". Proper correction is required.

Claims 22 and 23 are objected to for inconsistencies. Claims 22 and 23 recite: "…(SEQ ID NO: 2-6)…(SEQ ID NO: 6-11)…". Other than claims 22 and 23, the term "NOS" is recited before multiple sequences. The following amendment would obviate this objection: "…(SEQ ID NO**S**: 2-6)…(SEQ ID NO**S**: 6-11)…". Proper correction is required.

Claim 27 is objected to for reciting: "...wherein comparable alterations in levels of expression products..". Claims 27 is drawn to a method of comparing levels and not "alterations" in levels. Amending claim 27 in the following manner would obviate this objection: : "...wherein comparable ~~alterations in~~ levels of expression products..". Proper correction is required.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 5-8, 10, 11, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and dependent claims 2, 5-8, 10, and 11 are rejected because claim 1 recites: "the expression profile under test". While there is antecedent basis for "the expression profile", there is insufficient antecedent basis for "the expression profile under test" in the claim.

Claim 1 and dependent claims 2, 5-8, 10, and 11 are rejected because claim 1 recites: “the prognostic set of nucleic acid products”. There is insufficient antecedent basis for “the prognostic set of nucleic acid products" in the claim.

Claim 1 and dependent claims 2, 5-8, 10, and 11 are rejected because claim 1 recites: "has a poorer prognosis” without indicating as compared to what said prognosis is poorer. It is not clear from the claims or the specification what is meant by "poorer prognosis". This renders the claim indefinite because the term “poorer prognosis” is not defined by the claim and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Given the above reasons, the metes and bounds of the claims cannot be determined.

Claim 1 and dependent claims 2, 5-8, 10, and 11 are rejected because claim 1 recites: “…has a poorer prognosis as determined by comparison with said previously determined standard expression signature…”. It is not clear what is to be compared with said previously determined standard expression signature. Given the above reasons, the metes and bounds of the claims cannot be determined.

Claim 1 and dependent claims 2, 5-8, 10, and 11 are rejected because claim 1 recites: “the tumor sample”. While there is antecedent basis for “the breast tumor”, there is insufficient antecedent basis for “the tumor sample" in the claim.

Claim 10 recites: "The method of claim 9...". There is insufficient antecedent basis for this limitation in the claim. Claim 9 has been cancelled by Applicant.

Claims 11 and 27 recite: "…the expression levels of the prognostic set…". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8, 11, 12, 13, 16-20, 22 -27 are rejected under 35 U.S.C. 102(b) as being anticipated by Sorlie et al (PNAS, September 2001, 98(19):10869-10874).

Claims 1 and 2 are drawn to a method comprising obtaining an expression profile of nucleic acid products of a prognostic set of genes from a patient breast tumor sample, comparing the expression profile with a previously determined standard expression signature profile which is associated with low or high NPI, wherein a prognostic set of nucleic acid products comprises SEQ ID NOs:1-13. It is noted that claims 1 and 2 do not require the obtained expression profile of nucleic acid products to include any nucleic acids represented by SEQ ID NOs:1-13; rather, the obtained expression profile of nucleic acid products can be any nucleic acid products which could possibly be part of a prognostic set of genes comprising SEQ ID NOs:1-13. Claim 8 is

drawn to the method of claim 1, comprising classifying the sample of breast tumour as being either high NPI or low, or as either of good or bad prognosis NPI relative to a previously determined NPI expression signature profile. Claim 11 is drawn to the method of claim 1 further comprising comparing an expression level of a prognostic set in the breast tumour sample before and after treatment. Claims 12 and 13 are drawn to an apparatus comprising a solid support to which are attached a plurality of nucleic acid binding members, each binding member being capable of specifically and independently binding to an expression product of one or a prognostic set of genes, wherein the prognostic set of genes comprises SEQ ID NOs:1-13, and wherein said solid support houses nucleic acid binding members for not more than 500 different genes. It is noted that claims 12 and 13 do not require the apparatus comprise binding members that specifically bind to any nucleic acids represented by SEQ ID NOs:1-13; rather, the binding members of the apparatus can be binding members that bind any nucleic acid products which could possibly be part of a prognostic set of genes comprising SEQ ID NOs:1-13. Claims 16 and 17 are drawn to a kit comprising a plurality of nucleic acid binding members, each binding member being capable of specifically and independently binding to an expression product of one or a prognostic set of genes, wherein the prognostic set of genes comprises SEQ ID NOs:1-13, and wherein said kit comprises less than 500 binding members. It is noted that claims 16 and 17 do not require the kit comprise binding members that specifically bind to any nucleic acids represented by SEQ ID NOs:1-13; rather, the binding members of the kit can be binding members that bind any nucleic acid products which could possibly be

part of a prognostic set of genes comprising SEQ ID NOs:1-13. Claim 18 is drawn to the kit of claim 16, further comprising a data analysis tool, wherein the data analysis tool is a computer program. Claim 19 is drawn to the kit of claim 18 wherein the data analysis tool comprises an algorithm adapted to discriminate between the expression profiles of tumours with differing prognoses. Claim 20 is drawn to the kit of claim 16, comprising expression profiles from breast tumour samples with known prognoses and/or expression profiles characteristic of a particular prognosis. Claim 22 is drawn to a kit comprising a plurality of nucleic acid binding members, each binding member being capable of specifically and independently binding to an expression product of one or a prognostic set of genes, wherein the prognostic set of genes comprises SEQ ID NOs:1-13, and wherein said kit comprises less than 500 binding members, and wherein said binding members are nucleotide primers capable of binding to the nucleic acid expression products of the genes of the prognostic set such that the nucleic acid expression products can be amplified by PCR. It is noted that claim 22 does not require the kit comprise binding members that specifically bind to any nucleic acids represented by SEQ ID NOs:1-13; rather, the binding members of the kit can be binding members that bind any nucleic acid products which could possibly be part of a prognostic set of genes comprising SEQ ID NOs:1-13. Claims 23 and 24 are drawn to a method comprising isolated nucleic acid expression products from a breast tumor sample, identifying the expression levels of nucleic acid expression products of a prognostic set of genes wherein the prognostic set of genes comprises SEQ ID NO:1-13, and producing from the expression levels an expression profile for said breast tumour

sample. It is noted that claims 23 and 24 do not require identifying expression levels of nucleic acids represented by SEQ ID NOs:1-13; rather, the method requires identifying expression levels of nucleic acid products which could possibly be part of a prognostic set of genes comprising SEQ ID NOs:1-13. Claim 25 is drawn to the method of claim 23 comprising adding the expression profile to a gene expression profile databases. Claim 26 is drawn to the method of claim 23 further comprising comparing the expression profile with a second expression profile or a plurality of second expression profiles characteristic of a particular prognosis. Claim 27 is drawn to the method of claim 26, comprising the steps (a) isolating nucleic acid expression products from a first breast tumour sample, contacting said expression products with a plurality of binding members capable of specifically and independently binding to expression products of a prognostic set, and creating a first expression profile from the expression levels of the prognostic set in the tumour sample; (b) isolating nucleic acid expression products from a second breast tumor sample of known prognosis and known NPI status, contacting said expression products with a plurality of binding members capable of specifically and independently binding to expression products of the prognostic set of step (a), so as to create a second expression profile of a breast tumor sample; and (c) comparing the levels of expression products from said first and second expression profiles.

Sorlie et al teaches a method comprising obtaining an expression profile of nucleic acid products of a prognostic set of genes from a patient breast tumor sample, comparing the expression profile with a previously determined standard expression signature profile which is associated with low or high NPI, wherein a prognostic set of

nucleic acid products comprises SEQ ID NOs:1-13 (pages 10869-10870, in particular). Sorlie et al teaches said method further comprising classifying the sample of breast tumour, wherein said classifying could be described as being either high NPI or low, or as either of good or bad prognosis NPI relative to a previously determined NPI expression signature profile (Figure 1, in particular). It is noted that Sorlie et al does not use the term NPI; however, the instant claims do not limit as to what is to be required of an NPI expression profile. Sorlie et al further teaches said method further comprising comparing an expression level of a prognostic set in the breast tumour sample before and after treatment (Figure 3, in particular). Sorlie et al further teaches an apparatus comprising a solid support to which are attached a plurality of nucleic acid binding members, each binding member being capable of specifically and independently binding to an expression product of one or a prognostic set of genes, wherein the prognostic set of genes comprises SEQ ID NOs:1-13, and wherein said solid support houses nucleic acid binding members for not more than 500 different genes (see Figures 1 and 4, in particular). Sorlie et al further teaches a kit comprising a plurality of nucleic acid binding members, each binding member being capable of specifically and independently binding to an expression product of one or a prognostic set of genes, wherein the prognostic set of genes comprises SEQ ID NOs:1-13, and wherein said kit comprises less than 500 binding members (see Figures 1 and 4, in particular). Sorlie et al further teaches said kit further comprising a data analysis tool, wherein the data analysis tool is a computer program, wherein the data analysis tool comprises an algorithm adapted to discriminate between the expression profiles of tumours with

differing prognoses (left column of page 10870, in particular). Sorlie et al further teaches said kit further comprising expression profiles from breast tumour samples with known prognoses and/or expression profiles characteristic of a particular prognosis (see page 10870, in particular). Sorlie et al further teaches a kit comprising a plurality of nucleic acid binding members, each binding member being capable of specifically and independently binding to an expression product of one or a prognostic set of genes, wherein the prognostic set of genes can comprise SEQ ID NOs:1-13, and wherein said kit comprises less than 500 binding members, and wherein said binding members are nucleotide primers capable of binding to the nucleic acid expression products of the genes of the prognostic set such that the nucleic acid expression products can be amplified by PCR (see Figures 1 and 4, in particular). Sorlie et al further teaches a method comprising isolated nucleic acid expression products from a breast tumor sample, identifying the expression levels of nucleic acid expression products of a prognostic set of genes wherein the prognostic set of genes can comprise SEQ ID NO:1-13, and producing from the expression levels an expression profile for said breast tumour sample (Figure 1, in particular). Sorlie et al further teaches said method further comprising adding the expression profile to a gene expression profile databases and further comprising comparing the expression profile with a second expression profile or a plurality of second expression profiles characteristic of a particular prognosis (page 10870 and Figure 3, in particular). Sorlie et al further teaches said method comprising the steps (a) isolating nucleic acid expression products from a first breast tumour sample, contacting said expression products with a plurality of binding members

capable of specifically and independently binding to expression products of a prognostic set, and creating a first expression profile from the expression levels of the prognostic set in the tumour sample; (b) isolating nucleic acid expression products from a second breast tumor sample of known prognosis and known NPI status, contacting said expression products with a plurality of binding members capable of specifically and independently binding to expression products of the prognostic set of step (a), so as to create a second expression profile of a breast tumor sample; and (c) comparing the levels of expression products from said first and second expression profiles (page 10870 and Figure 3, in particular). It is noted that the "known" prognosis and NPI status is an inherent property of a breast tumor sample.

Allowable Subject Matter

Claim 14 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Examiner, Art Unit 1642